IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Henry WINDLE et al

Serial No.: New

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For: *CLOSTRIDIUM DIFFICILE* VACCINE

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE CLAIMS

Please cancel originally filed claims 1-66 without prejudice or disclaimer.

Please add new claims 67-132 as follows.

Claims

67. A vaccine for the treatment or prophylaxis of *C. difficile* associated disease, the vaccine comprising a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans.

68. A vaccine for the treatment or prophylaxis of *C. difficile* associated disease, the vaccine comprising a *C. difficile* gene or *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof to which immunoreactivity is detected in individuals who have recovered from *C. difficile* infection.

69. A vaccine as claimed in claim 67 wherein the gene encodes a *C. difficile* surface layer protein, SlpA or variant or homologue thereof.

70. A vaccine as claimed in claim 67 wherein the peptide/polypeptide is a *C. difficile* surface layer protein, SlpA or variant or homologue thereof.

71. A vaccine as claimed in claim 67 wherein the vaccine comprises a chimeric nucleic acid sequence.

72. A vaccine as claimed in 71 wherein the chimeric nucleic acid sequence is derived from the 5' end of the gene, encoding the mature N-terminal moiety of SlpA from *C. difficile*.

73. A vaccine as claimed in claim 67 wherein the vaccine comprises a chimeric peptide/polypeptide.

74. A vaccine as claimed in 73 wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlpA from *C. difficile*.

75. A vaccine as claimed in claim 67 wherein the vaccine contains an amino acid sequence SEQ ID No.1 or a derivative or fragment or mutant or variant thereof.

76. A vaccine as claimed in claim 67 wherein the vaccine contains an amino acid sequence SEQ ID No.2 or a derivative or fragment or mutant or variant thereof.

77. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.3 or a derivative or fragment or mutant or variant thereof.

78. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.4 or a derivative or fragment or mutant or variant thereof.

79. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.5 or a derivative or fragment or mutant or variant thereof.

80. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.6 or a derivative or fragment or mutant or variant thereof.

81. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.7 or a derivative or fragment or mutant or variant thereof.

82. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.8 or a derivative or fragment or mutant or variant thereof.

83. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.9 or a derivative or fragment or mutant or variant thereof.

84. A vaccine as claimed in claim 67 wherein the vaccine contains a nucleotide sequence SEQ ID No.10 or a derivative or fragment or mutant or variant thereof.

85. A vaccine as claimed in claim 67 in combination with at least one other *C. difficile* sub-unit.

86. A vaccine for the treatment or prophylaxis of *C. difficile* associated disease, the vaccine comprising the mature N-terminal moiety of a surface layer protein, SlpA of *C. difficile* or variant or homologue thereof which is immunogenic in humans.

87. A vaccine as claimed in claim 86 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 1.

88. A vaccine as claimed in claim 86 wherein the N-terminal moiety of SlpA contains an amino acid sequence SEQ ID No. 2.

89. A vaccine for the treatment or prophylaxis of *C. difficile* associated disease, the vaccine comprising an immunodominant epitope derived from a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans.

90. A vaccine as claimed in claim 67 comprising a pharmaceutically acceptable carrier.

91. A vaccine as claimed in claim 67 in combination with a pharmacologically suitable adjuvant.

92. A vaccine as claimed in claim 91 wherein the adjuvant is interleukin 12.

93. A vaccine as claimed in claim 91 wherein the adjuvant is a heat shock protein.

94. A vaccine as claimed in claim 67 comprising at least one other pharmaceutical product.

95. A vaccine as claimed in claim 94 wherein the pharmaceutical product is an antibiotic.

96. A vaccine as claimed in claim 95 wherein the antibiotic is selected from one or more metronidazole, amoxycillin, tetracycline or erythromycin, clarithromycin or tinidazole.

97. A vaccine as claimed in claim 94 wherein the pharmaceutical product comprises an acid-suppressing agent such as omeprazole or bismuth salts.

98. A vaccine as claimed in claim 67 in a form for oral administration.

99. A vaccine as claimed in claim 67 in a form for intranasal administration.

100. A vaccine as claimed in claim 67 in a form for intravenous administration.

101. A vaccine as claimed in claim 67 in a form for intramuscular administration.

102. A vaccine as claimed in claim 67 including a peptide delivery system.

103. An immunodominant epitope derived from a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof.

104. An immunodominant epitope as claimed in claim 103 wherein the *C. difficile* peptide/polypeptide contains an amino acid sequence SEQ ID No.1 or SEQ ID No.2 or a derivative or fragment or mutant or variant thereof.

105. An immunodominant epitope as claimed in claim 101 wherein the *C. difficile* peptide/polypeptide contains an amino acid sequence SEQ ID No.3 or SEQ ID No.4 or SEQ ID No.5 or SEQ ID No.6 or SEQ ID No.7 or SEQ ID No.8 or SEQ ID No. 9 or SEQ ID No. 10 or a derivative or fragment or mutant or variant thereof.

106. A chimeric nucleic acid sequence derived from the 5' end of the slpA gene encoding the mature N-terminal moiety of SlpA from *C. difficile* which is immunogenic in humans.

107. A chimeric peptide/polypeptide wherein the amino acid sequence of the chimeric peptide/polypeptide is derived from the mature N-terminal moiety of SlpA from *C. difficile*.

108. A *C. difficile* peptide comprising SEQ ID No. 1.

109. A *C. difficile* peptide comprising SEQ ID No. 2.

110. A *C. difficile* gene comprising SEQ ID No. 3.

111. A *C. difficile* gene comprising SEQ ID No. 4.

112. A *C. difficile* gene comprising SEQ ID No. 5.

113. A *C. difficile* gene comprising SEQ ID No. 6.

114. A *C. difficile* gene comprising SEQ ID No. 7.

115. A *C. difficile* gene comprising SEQ ID No. 8.

116. A *C. difficile* gene comprising SEQ ID No. 9.

117. A *C. difficile* gene comprising SEQ ID No. 10.

118. The use of a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans in the preparation of a medicament for use in a method for the treatment or prophylaxis of *C. difficile* infection or *C. difficile* associated disease in a host.

119. The use as claimed in claim 118 wherein the medicament which is prepared is a vaccine.

120. A method for preparing a vaccine for prophylaxis or treatment of *C. difficile* associated disease, the method comprising;

obtaining a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans; and

forming a vaccine preparation comprised of said gene or peptide/polypeptide or derivative or fragment or mutant or variant, which is suitable for administration to a host and which when administered raises an immune response.

121. A method as claimed in claim 120 wherein the *C. difficile* peptide/polypeptide contains an amino acid sequence SEQ ID No.1 or SEQ ID No.2 or a derivative or fragment or mutant or variant thereof.

122. A method as claimed in claim 120 wherein the *C. difficile* gene contains an amino acid sequence SEQ ID No.3 or SEQ ID No.4 or SEQ ID No.5 or SEQ ID No.6 or SEQ ID No.7 or SEQ ID No.8 or SEQ ID No.9 or SEQ ID No.10 or a derivative or fragment or mutant or variant thereof.

123. A method for prophylaxis or treatment of *C. difficile* associated disease, the method comprising;

obtaining a *C. difficile* gene or a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans;

forming a vaccine preparation comprised of said gene or peptide/polypeptide or derivative or fragment or mutant or variant, and

administering the vaccine preparation to a host to raise an immune response.

124. Monoclonal or polyclonal antibodies or fragments thereof, to a *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans.

125. Monoclonal or polyclonal antibodies or fragments thereof, to *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof to which immunoreactivity is detected in individuals who have recovered from *C. difficile* infection.

126. Purified antibodies or serum obtained by immunisation of an animal with a vaccine according to claim 67.

127. The use of the antibodies or fragments as claimed in claim 124 in the preparation of a medicament for treatment or prophylaxis of *C. difficile* infection or *C. difficile* associated disease.

128. The use of the antibodies or serum as claimed in 126 in the preparation of a medicament for treatment or prophylaxis of *C. difficile* infection or *C. difficile* associated disease.

129. The use of the antibodies or fragments or serum as claimed in claim 124 for use in passive immunotherapy for established *C. difficile* infection.

130. The use of the antibodies or fragment or serum as claimed in claim 124 for the eradication of *C. difficile* associated disease.

131. Use of interleukin 12 as an adjuvant in *C. difficile* vaccine.

132. The use of humanised antibodies or serum for passive vaccination of an individual with *C. difficile* infection.

REMARKS

The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee.

Early action on the merits is respectfully requested.

Respectfully submitted,

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